Microfluidics Session-15

This image depicts **droplet operations in a digital fluidic circuit**. Each frame represents a distinct process involved in the manipulation of droplets within a microfluidic system. Here's a brief explanation of the operations shown:

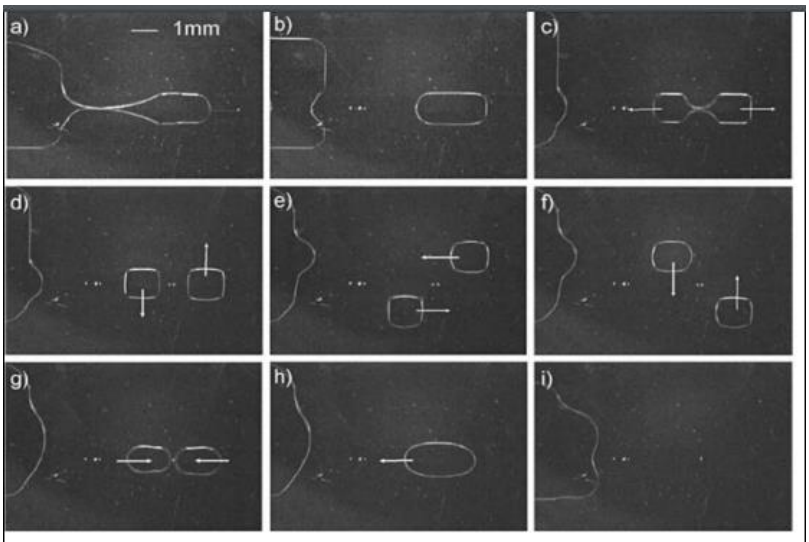
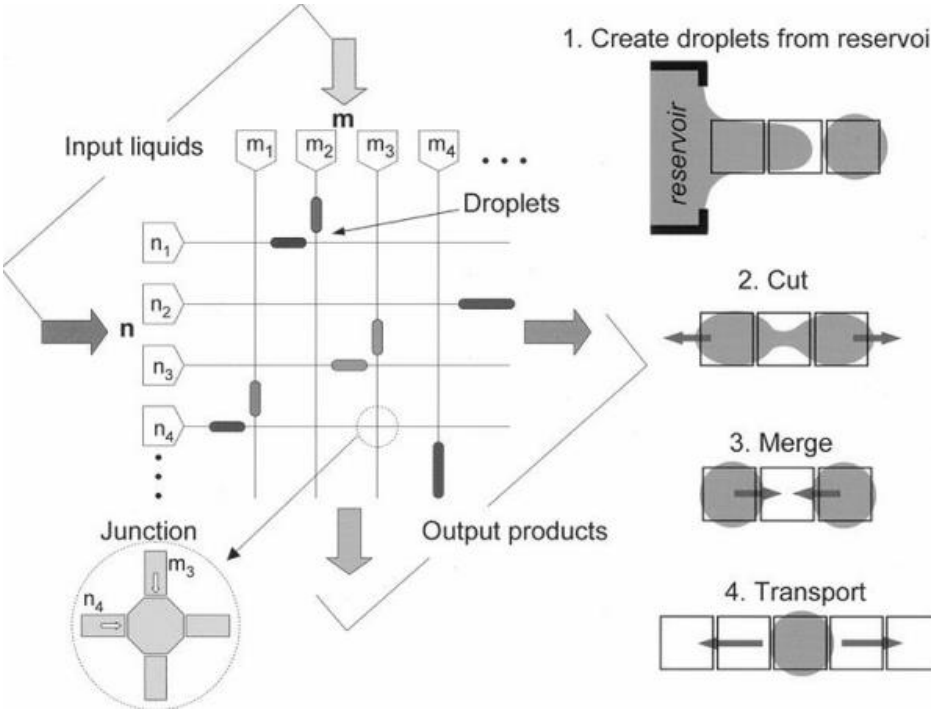


FIG. 1.3: Droplet operations in digital fluidic circuit. (a) and (b) Droplet creation from reservoir; (c) droplet cutting; (d)–(f) simultaneous and independent transport of two droplets; (g)–(i) merging of the droplets and return to reservoir. (Reprinted with permission from Fan *et al.* 2003 Copyright 2003, IEEE).

1. **Droplet Creation (a and b)**: Droplets are generated from a reservoir. This process involves breaking a liquid column into discrete droplets.
2. **Droplet Cutting (c)**: A single droplet is divided into smaller droplets, a critical step for precise control of fluid volumes in microfluidic applications.
3. **Simultaneous and Independent Transport (d–f)**: Two droplets are transported independently through the circuit. This demonstrates the ability to control multiple droplets without interference.
4. **Droplet Merging and Return to Reservoir (g–i)**: Two droplets are merged into one and then directed back to the reservoir. This operation is essential for mixing fluids or combining reagents in microfluidic assays.

These processes demonstrate the flexibility and precision of digital microfluidic systems in handling fluids at micro and nanoscales for applications such as biological assays, chemical synthesis, and diagnostics (Micro_Nano Technology S…).

Digital Microfluidics • Digital microfluidics is a name given to a secondgeneration Lab-on-a-Chip architecture based upon micromanipulation of discontinuous fluid droplets. •The basic operations required in digital microfluidics include droplet formation, droplet translocation, droplet splitting, and merging.



This diagram represents a **digital microfluidic system** used for handling and processing droplets. It shows:

1. **Droplet Creation**: Liquid from reservoirs (n1, n2, etc.) is converted into droplets (m1, m2, etc.).
2. **Droplet Cutting**: Larger droplets are split into smaller ones for precise volume control.
3. **Droplet Merging**: Two droplets are combined at junctions for mixing or reactions.
4. **Droplet Transport**: Droplets are moved across the grid to specific locations.

This system enables precise, programmable operations for biological assays, chemical reactions, and diagnostics.

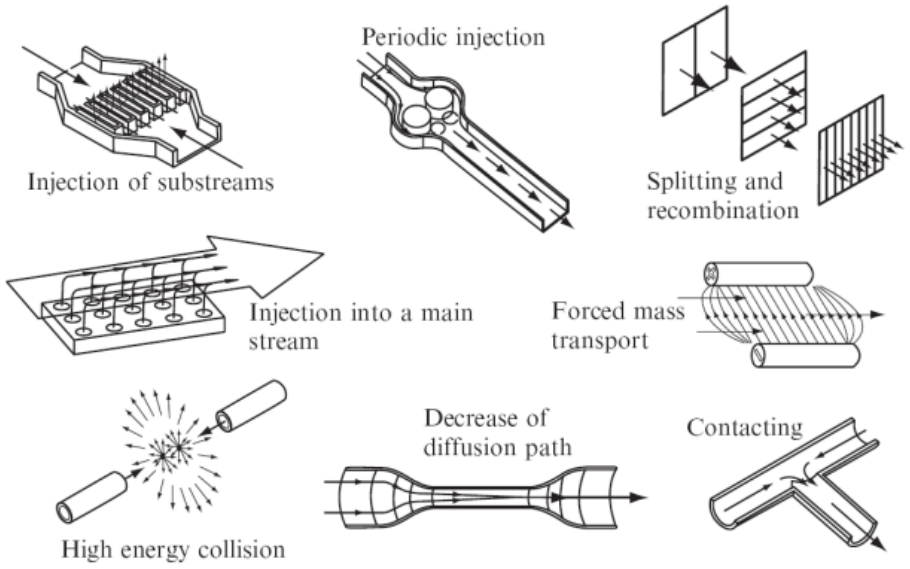


FIG. 2.1: Schematic diagrams of typical strategies to achieve passive and active micromixing. Hessel *et al.* (2005).

This schematic shows **strategies for passive and active micromixing** in microfluidic systems, as described by Hessel et al. (2005). Here's a brief overview:

1. **Injection of Substreams**: Dividing the flow into multiple small streams to increase interaction.
2. **Periodic Injection**: Alternating injections of fluids to enhance mixing.
3. **Splitting and Recombination**: Dividing a stream and recombining it to improve diffusion.
4. **Injection into a Main Stream**: Introducing secondary fluids into a primary stream for mixing.
5. **Forced Mass Transport**: Using external forces (e.g., pressure or flow) to accelerate mixing.
6. **High-Energy Collision**: Colliding streams to create turbulent mixing.
7. **Decrease of Diffusion Path**: Reducing the distance molecules must diffuse to mix efficiently.
8. **Contacting**: Bringing streams into direct contact for mixing.

These strategies are used to improve the efficiency of mixing at micro and nano scales for biological and chemical processes.

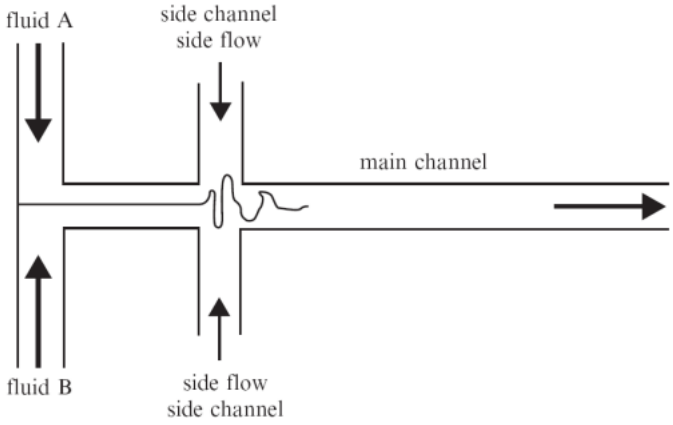
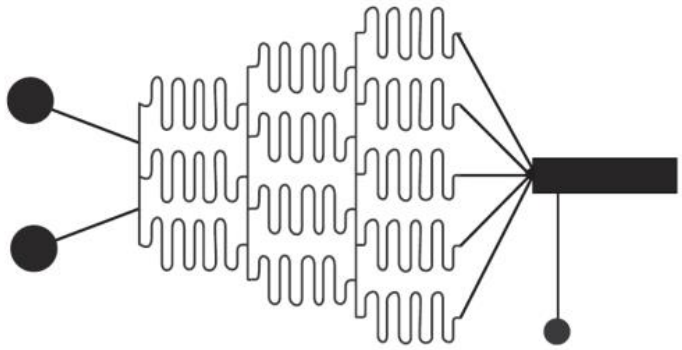


FIG. 2.2: Stretching/folding micromixer proposed by Lee *et al.* (2002).

This figure illustrates a **stretching/folding micromixer** proposed by Lee et al. (2002). It shows:

- **Fluid A and Fluid B**: Two fluids entering the mixer from opposite sides.
- **Side Channels**: Additional flows introduced from side channels to create disturbances.
- **Main Channel**: The fluids are stretched and folded as they move through the main channel, enhancing mixing by reducing the diffusion path.

This design improves the efficiency of mixing in microfluidic systems by leveraging stretching and folding mechanisms to create better contact between fluids.



G. 2.8: System allowing five chambers (on the right side) incorporating solutions at five different concentrations. The system is fed by the two entries shown on the left side (Jeon *et al.* 2002).

This figure shows a **microfluidic system** designed to create five chambers with solutions of **five different concentrations**, as described by Jeon et al. (2002). Key points:

- **Two Inputs**: The system is fed by two entry points on the left, introducing different solutions or fluids.
- **Branching Network**: A series of interconnected channels mix and distribute the fluids to create a gradient of concentrations.
- **Output Chambers**: Five chambers on the right collect the solutions, each having a unique concentration.

This system is commonly used for applications like gradient generation in chemical or biological experiments, such as studying cell responses to varying concentrations of a stimulus.

This figure illustrates a droplet-based microfluidic system for conducting microreactions, as described by Song et al. (2003). Key features:

Reagents A and B: Two reagents are introduced into the system, separated by an immiscible stream of oil to prevent dispersion.
Rapid Mixing: The reagents are rapidly mixed within a winding channel, which enhances the reaction efficiency.
Controlled Microenvironment: The droplet-based system ensures no cross-contamination and maintains precise control over reaction conditions.
This setup is widely used in chemical and biological experiments to perform highly controlled microreactions with minimal reagent use.

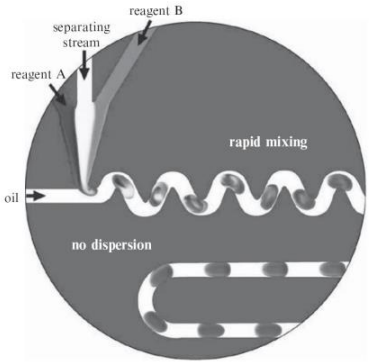


FIG. 2.9: A typical droplet-based microfluidic system to carry out microreactions (Song *et al.* 2003).

This figure illustrates a **droplet-based microfluidic system** for conducting microreactions, as described by Song et al. (2003). Key features:

- **Reagents A and B**: Two reagents are introduced into the system, separated by an immiscible stream of oil to prevent dispersion.
- **Rapid Mixing**: The reagents are rapidly mixed within a winding channel, which enhances the reaction efficiency.
- **Controlled Microenvironment**: The droplet-based system ensures no cross-contamination and maintains precise control over reaction conditions.

This setup is widely used in chemical and biological experiments to perform highly controlled microreactions with minimal reagent use.

Microfluidics - Motivation

- Sophisticated chemical and biological analytical procedures, such as those used in medical diagnosis and environmental monitoring, have traditionally been conducted in dedicated laboratories by highly trained personnel.
- These protocols are typically performed on bench tops using test tubes and beakers.
- This bench-top norm imposes limitations such as restricted accessibility, lengthy turnaround times, complex logistics (e.g., sample transportation and storage), and high costs.

Microfluidics - Motivation

- Over the past few decades, integrated circuits have revolutionized the landscape of traditional electronics.
- The exponential increase in performance and reduction in cost are direct results of miniaturizing components, fabricating them using monolithic integration methods, and connecting them on a massive scale.
- Can we reduce the size of test tubes, beakers, and channels? Can we create an integrated, low-cost system capable of performing complex biological and chemical protocols without human intervention, in a fully automated manner?
- If the answers to these questions are “yes,” then perhaps the same benefits realized by the microelectronics industry can also transform biology, chemistry, and medicine.

Microfluidics System - Defined

- A microfluidics system for chemical and biological diagnosis is commonly referred to as a “laboratory-on-a-chip” or a “micro total analysis system” (mTAS).

Microfluidics System - Explained

- Just as microelectronic circuits revolutionized signal processing and communication, fluid reactions conducted within integrated, miniaturized microfluidic channels and reactors hold the potential to transform practices in:
    - Medical diagnosis and intervention,
    - Drug discovery,
    - Environmental monitoring,
    - Cell culture and manipulation of bioparticles,
    - Gas handling and analysis (e.g., component separation or heat transfer),
    - Heat exchange,
    - Chemical reactors (for power and force production), and
    - Bioterrorism defense.

Microfluidics - Advantages

- A microfluidics system reduces dead volumes associated with chemical assay systems that use large-scale chambers and connectors.
- It decreases the amount of chemical assays and solutions required, potentially reducing costs by saving on expensive chemicals and biological samples used for a given analysis.
- Microelectronics-style bulk fabrication methods can further lower the cost of sophisticated systems.
- Lithography and parallel fabrication simplify the construction of complex fluid piping and reaction networks.
- Microfluidics enables high levels of multiplexing and parallel operations, increasing the efficiency of chemical and biological discovery.

Microfluidics Actuation Methods

1. **Pressure Difference**:
    - Pressure differences can be generated in various ways (as outlined in Section 13.3.3). Both positive pressure (upstream) and negative pressure (downstream) can be used to pump fluids.
    - The simplest method to create a pressure head in a laboratory is by using an elevated liquid reservoir relative to the level of the fluid outlet.
2. **Magnetohydrodynamic (MHD) Effect**:
    - The MHD effect involves the flow of electrically conducting liquids in the presence of electrical and magnetic fields [33].
    - In an MHD pump, an electric field and a magnetic field are applied simultaneously, transverse to the fluid channel and perpendicular to each other.
    - The electric field induces movement of the conducting liquid within the magnetic field.

3. **Electrohydrodynamic Effect**:
    - This effect utilizes the interaction of an electric field with electric charges embedded in a dielectric fluid [34–37].
    - Charges or charged particles can be injected directly or by adding a liquid with a high density of ions.

Microfluidics Actuation Methods

- **Magnetorheological Pumping**:
    - Involves moving plugs of ferrofluid using magnetic actuation. A ferrofluid is a liquid solution containing a suspension of nanosized ferromagnetic particles.
- **Surface Tension-Driven Flow**:
    - Surface tension force is relatively large at the microscale compared to other forces, such as gravity or structural restoring forces.
    - It can be used to move liquid in capillaries or manipulate liquid drops on a planar surface. For example, the surface tension at the liquid-substrate interface can be altered by applying electrical charges, a phenomenon known as electrowetting.

Microfluidics Actuation Methods

- **Traveling Surface Acoustic Waves**:
    - These waves can be used to stream liquid in contact with the substrate.
- **Electroosmotic Effect (EO)**:
    - Refers to the motion of bulk liquid caused by the application of an electrical field parallel to a channel with charged walls.

Factors to Consider for On-Chip Pump Selection

When selecting technologies for on-chip pumps, several important factors must be considered, including:

- Achievable flow rate,
- Simplicity of fabrication,
- Cost of fabrication,
- Simplicity of control,
- Robustness of the membrane,
- Biocompatibility of the membrane and channel materials, and
- Energy consumption, which is critical for portable systems.

Selection of Components in Microfluidics

- Microfluidic channels are the most important components in a microfluidic system, despite their relatively simple form and function compared to others (such as pumps and valves).
- The selection of channel material is the starting point for any development effort in microfluidic systems. Several important aspects must be considered when selecting channel materials and subsequent fabrication methods, including:

1. **Hydrophobicity of the Channel Wall**:
    - Liquid moves freely in channels with hydrophilic walls due to capillary action, simplifying sample loading and priming.
    - For example, glass is hydrophilic to many liquids, and its properties are well established.
    - Introducing liquid into channels with hydrophobic walls, however, is considerably more difficult.
2. **Biocompatibility and Chemical Compatibility**:
    - Ideally, the channel wall should not react with the fluid, particles, or gases within.
    - Glass, commonly used for beakers and test tubes, is one of the most established biocompatible materials and is highly regarded by researchers in biology and chemistry.
    - However, a major drawback is the lack of micromachining methods for glass.

Selection of Components in Microfluidics

- **Permeability of Channel Material to Air and Liquid**:
    - High permeability can cause excessive fluid loss or, in cases where multiple channels are placed close together, cross-contamination.
    - However, the permeability of air or gas can be advantageous for air escape and the removal of trapped air bubbles.
- **Retention of Chemicals on Walls**:
    - Walls that retain chemicals may lead to cross-contamination during repeated use.
- **Optical Transparency**:

    - Optically transparent walls facilitate observation and enable quantitative assay analysis.
- **Temperature of the Processing**:
    - Low-temperature processing is always desirable.
    - High-temperature processes narrow the choice of structural and surface coating materials.
- **Functional Complexity and Development Cost**:
    - The materials used for channels should be amenable to the integration of active components, such as pumps and valves.
    - The barriers to prototyping and manufacturing should be minimal.

Materials for Microfluidic Channels

- **Organic Polymers**:
    - Parylene
    - Polydimethylsiloxane (PDMS)
    - Acrylics
    - Polycarbonate
    - Biodegradable polymer
    - Polyimide
- **Inorganic Materials**:
    - Glass (e.g., Pyrex, specialty glasses)
    - Silicon
    - Silicon dioxide
    - Silicon nitride
    - Polysilicon

Problem 1: Design

For a microfluid channel with a length of 1 mm, and a square cross-sectional area of 20 μm^2, find the volumetric flow and average flow speed if one end of the channel is subjected to a water column that is 5 m tall. The other end is connected to atmosphere pressure.

$$Q = \frac{\pi r^4 \Delta P}{8 \mu L}$$

Where:

- Q = Volumetric flow rate (m^3/s)
- r = Radius of the channel (in meters)
- ΔP = Pressure difference (in Pascals)
- μ = Viscosity of water ($1 \times 10^{-3}\,\mathrm{Pa\cdot s}$)
- L = Length of the channel (in meters)

$$v = \frac{Q}{A}$$

Where:

- v = Average flow speed (m/s)
- A = Cross-sectional area of the channel (m^2)

Step-by-Step Solution:

1. Given Data:
    - Length of channel (L) = $1\,\mathrm{mm} = 0.001\,\mathrm{m}$
    - Cross-sectional area (A) = $20\,\mu\mathrm{m}^2 = 20 \times 10^{-12}\,\mathrm{m}^2$
    - Water column height = $5\,\mathrm{m}$
    - Density of water (ρ) = $1000\,\mathrm{kg}/\mathrm{m}^3$
    - Gravitational acceleration (g) = $9.81\,\mathrm{m}/\mathrm{s}^2$
    - Viscosity (μ) = $0.001\,\mathrm{Pa\cdot s}$
2. Calculate Pressure Difference (ΔP):

$$\Delta P = \rho \cdot g \cdot h$$

Substituting:

$$\Delta P = 1000 \cdot 9.81 \cdot 5 = 49050\,\text{Pa}$$

3. Calculate Radius (r):
   The cross-sectional area (A) is related to the radius by:

$$A = \pi r^2 \quad \text{so} \quad r = \sqrt{\frac{A}{\pi}}$$

   Substituting:

$$r = \sqrt{\frac{20 \times 10^{-12}}{\pi}} = 2.52 \times 10^{-6}\,\text{m}$$

4. Calculate Volumetric Flow Rate (Q):
   Using the Hagen-Poiseuille equation:

$$Q = \frac{\pi r^4 \Delta P}{8 \mu L}$$

   Substituting:

$$Q = \frac{\pi (2.52 \times 10^{-6})^4 (49050)}{8(0.001)(0.001)}$$

   Simplify:

$$Q = 7.81 \times 10^{-13}\,\text{m}^3/\text{s}$$

5. Calculate Average Flow Speed (v):
   Using:

$$v = \frac{Q}{A}$$

   Substituting:

$$v = \frac{7.81 \times 10^{-13}}{20 \times 10^{-12}} = 0.039\,\text{m/s}$$

Final Results:

- Volumetric Flow Rate (Q): $7.81 \times 10^{-13}\,\text{m}^3/\text{s}$
- Average Flow Speed (v): $0.039\,\text{m/s}$

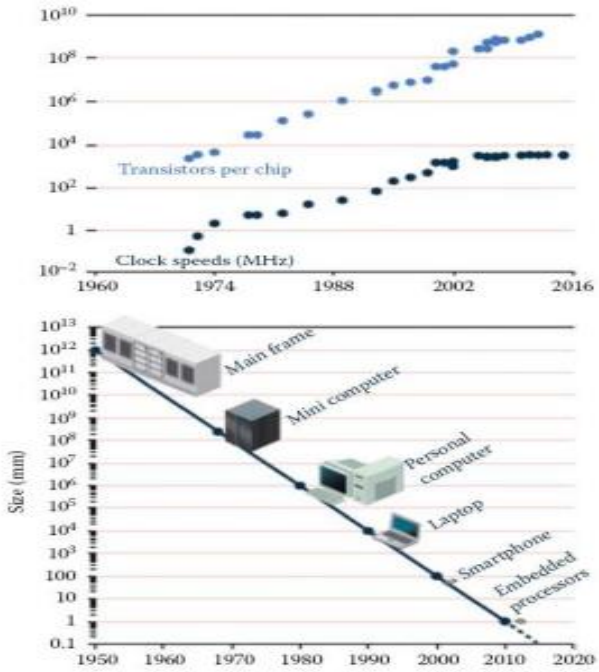


FIGURE 1.1
Miniaturization of electronic devices according to Moore's law since 1970 and its saturation. (Reprinted by permission from Springer Nature. *Nature*, Waldrop M. More than Moore. 530: 144–147, copyright 2016.)

This figure illustrates the **miniaturization of electronic devices** over time, following **Moore's Law** and its eventual saturation:

1. **Top Graph**:
   - Shows the exponential increase in **transistors per chip** (y-axis) since 1970, demonstrating Moore's Law.
   - **Clock speeds (MHz)** grew significantly but began saturating around the 2000s due to physical and thermal limitations.
2. **Bottom Graph**:
   - Tracks the **size reduction** of electronic devices from mainframes in the 1950s to embedded systems and smartphones by 2020.
   - Highlights a continuous decline in size as technology evolved, showcasing trends in miniaturization.

This progression emphasizes how advancements in micro and nanotechnology have led to smaller, faster, and more efficient devices, driving innovations in various fields, including biomedical applications.

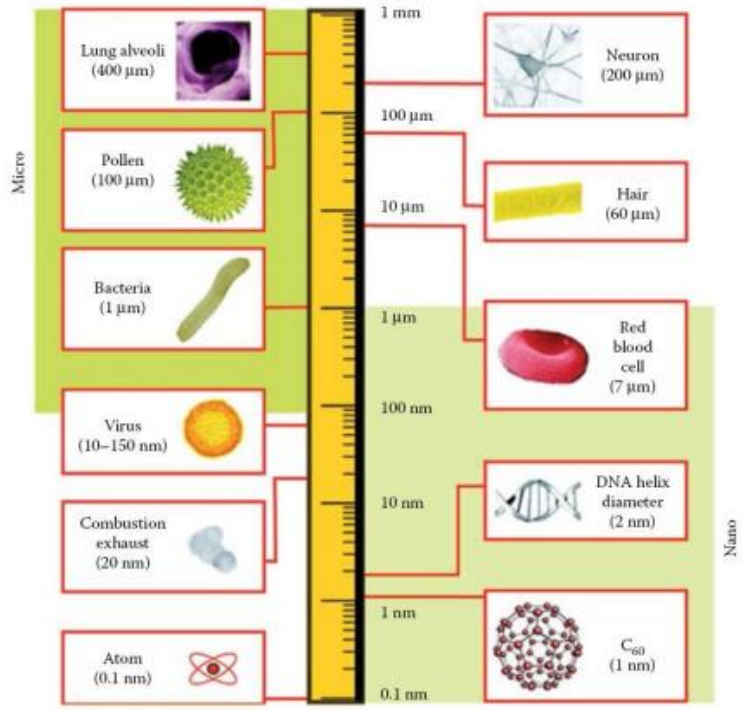


FIGURE 1.3
Logarithmical length scale showing size of nanomaterials compared to biological species. (From Buzea C., Pacheco I. I., Robbie K. 2007. *Biointerphases*. 2(4): 17–71. Open access.)

This figure presents a **logarithmic length scale** comparing the sizes of nanomaterials with biological species:

1. **Micrometer Scale**:
    - **Lung alveoli**: 400 µm
    - **Neuron**: 200 µm
    - **Pollen**: 100 µm
    - **Hair**: 60 µm
    - **Bacteria**: 1 µm
    - **Red blood cell**: 7 µm
2. **Nanometer Scale**:
    - **Virus**: 10–150 nm
    - **Combustion exhaust particles**: 20 nm
    - **DNA helix diameter**: 2 nm
    - **C_{60} molecule** (Buckyball): 1 nm
    - **Atom**: 0.1 nm

Significance:
This scale bridges the **micro** and **nano** worlds, illustrating the overlap between biological structures and synthetic nanomaterials. It emphasizes how nanotechnology operates at the same scale as many biological components, enabling advancements in biomedical applications such as drug delivery and diagnostics.

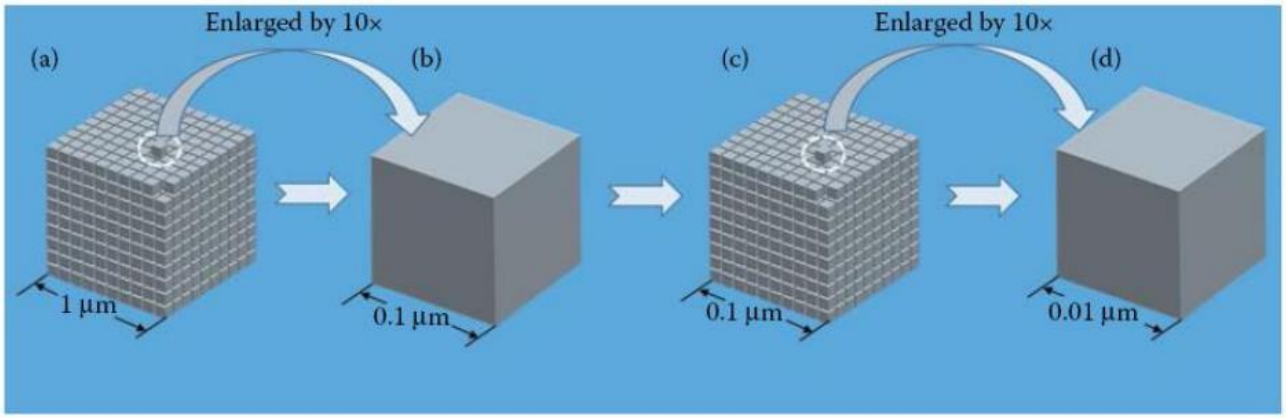


FIGURE 2.1
The division of parent cube with edge length of 1 μm into (a) smaller cubes with edge lengths of 0.1 μm and (c) 0.01 μm. The images in (b and d) show magnified view of 1/10th size of original cube shown in (a) and (c), respectively.

This figure illustrates the **division of a parent cube** with an edge length of 1 μm into progressively smaller cubes:

1. **Parent Cube (a)**:
   - Initial cube with a **1 μm** edge length.
   - Divided into smaller cubes with an edge length of **0.1 μm**.
2. **Magnified View (b)**:
   - A **10x enlarged view** of one smaller cube (edge length: 0.1 μm).
3. **Further Division (c)**:
   - The smaller cubes (0.1 μm) are further divided into cubes with an edge length of **0.01 μm**.
4. **Magnified View (d)**:
   - A **10x enlarged view** of one even smaller cube (edge length: 0.01 μm).

Significance:
This process highlights the concept of **scaling and miniaturization**, fundamental to micro and nanotechnology. It demonstrates how dividing a structure into smaller units increases surface area and enables precise manipulation at the micro and nano scales, which is critical for applications like drug delivery and material engineering.

EXAMPLE 3

How many CdSe unit cells are in a spherical particle with size (radius) of 12 Å, if the side of unit cell is 6.05 Å?

Solution

$$\text{Number of approximate unit cells of CdSe} = \left(\frac{\text{Volume of the spherical particle}}{\text{Volume of the CdSe unit cell}}\right)$$

$$= \left(\frac{(4/3)\pi r^3}{l^3}\right) = \left(\frac{(4/3)\times\pi\times 12^3}{6.05^3}\right) \simeq 4$$

This example calculates the number of CdSe unit cells in a spherical particle with a radius of $12\,\text{Å}$, given that the side of the unit cell is $6.05\,\text{Å}$.

Solution Outline:

1. Formula Used:

$$\text{Number of Unit Cells} = \frac{\text{Volume of the Spherical Particle}}{\text{Volume of the Unit Cell}}$$

The volume of the spherical particle is $\frac{4}{3}\pi r^3$, and the volume of the unit cell is l^3, where $l = 6.05\,\text{Å}$.

2. Substitution:

$$\text{Number of Unit Cells} = \frac{\frac{4}{3}\pi(12)^3}{(6.05)^3}$$

3. Calculation:

- Volume of the sphere: $(4/3)\pi(12)^3 = 7238.23\,\text{Å}^3$
- Volume of the unit cell: $(6.05)^3 = 221.48\,\text{Å}^3$
- Number of unit cells: $\frac{7238.23}{221.48} \approx 4$.

EXAMPLE 4

How many CdSe unit cells are in a cubical particle with size of 115 Å, if the edge length of the unit cell is 6.05 Å and it has the zinc-blende structure?

Solution

$$\text{Number of approximate unit cells of CdSe} = \left(\frac{\text{Volume of the cubical particle}}{\text{Volume of the CdSe unit cell}}\right)$$
$$= \left(\frac{L^3}{l^3}\right) = \left(\frac{115^3}{6.05^3}\right) \simeq 6868$$

This example calculates the number of CdSe unit cells in a cubical particle with an edge length of $115\,\text{Å}$, given that the edge length of the CdSe unit cell is $6.05\,\text{Å}$ (zinc-blende structure).

Solution Outline:

1. Formula Used:

$$\text{Number of Unit Cells} = \frac{\text{Volume of the Cubical Particle}}{\text{Volume of the Unit Cell}}$$

The volume of the cubical particle is L^3, and the volume of the unit cell is l^3, where $L = 115\,\text{Å}$ and $l = 6.05\,\text{Å}$.

2. Substitution:

$$\text{Number of Unit Cells} = \frac{115^3}{6.05^3}$$

3. Calculation:

- Volume of the cubical particle: $115^3 = 1520875\,\text{Å}^3$
- Volume of the unit cell: $6.05^3 = 221.48\,\text{Å}^3$
- Number of unit cells: $\frac{1520875}{221.48} \approx 6868$.

EXAMPLE 5

How many CdSe unit cells are in cubic crystal with an edge length of 100 μm? If the edge length of the unit cell is 6.05 Å.

Solution

$$\text{Number of approximate unit cells of CdSe} = \left(\frac{\text{Volume of the cubical crystal}}{\text{Volume of the CdSe unit cell}}\right)$$

$$= \left(\frac{L}{l}\right)^3 = \left(\frac{10^6}{6.05}\right)^3 = 4.515 \times 10^{15}$$

This example calculates the number of CdSe unit cells in a cubic crystal with an edge length of $100\ \mu m$, given that the edge length of the CdSe unit cell is $6.05\ \text{Å}$.

Solution Outline:

1. Formula Used:

$$\text{Number of Unit Cells} = \frac{\text{Volume of the Cubical Crystal}}{\text{Volume of the Unit Cell}}$$

The volume of the cubical crystal is L^3, and the volume of the unit cell is l^3, where $L = 10^6\ \text{Å}$ (since $100\ \mu m = 10^6\ \text{Å}$) and $l = 6.05\ \text{Å}$.

2. Substitution:

$$\text{Number of Unit Cells} = \left(\frac{L}{l}\right)^3 = \left(\frac{10^6}{6.05}\right)^3$$

3. Calculation:

- $\frac{10^6}{6.05} = 165289.26$
- $(165289.26)^3 = 4.515 \times 10^{15}$